The Texas Birth Defects
MONITOR
A Semi-Annual Data and Research Update

TEXAS
Department of State Health Services
Birth Defects Epidemiology and Surveillance

Volume 14, Issue 2 December 2008

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Research Symposium Proceedings

On October 17, 2008, researchers from around the state met in Lubbock to present recent findings on emerging birth defect patterns and prevalence, risk factors, prevention, and access to services. The following abstracts summarize the findings presented in the oral presentation portion of the event. Poster presentation abstracts can be found at our website, www.dshs.state.tx.us/birthdefects/conf_main.shtm

Selected Oral Presentation Abstracts

Recent findings on Gastroschisis in Texas. Presenter: Bonna Benjamin, M.D., Department of Pediatrics, TTUHSC Amarillo

Gastroschisis is a congenital abdominal wall defect that allows uncovered intestine to escape from the abdominal cavity and float freely in the amniotic space. The condition is easily identified prenatally and obvious at birth. Worldwide prevalence seems to be on the increase with geographic clusters of greater increase or absence of change. Maternal factors that have been associated with an increased risk of gastroschisis include young age, thin habitis, smoking, vasoactive medication use, race/ethnicity, and rural residence.

We determined the prevalence and predictors of gastroschisis in Texas using multivariate analysis. Gastroschisis was found to be more likely to occur among young, nulliparous mothers, even when accounting for other variables. African American mothers are at lower risk. A higher rate in Nueces County was the only significant geographic pattern.

The association between maternal fish consumption and birth defects. Presenter: Tunu A. Ramadhani, Ph.D., Texas Birth Defects Epidemiology and Surveillance Branch

Maternal fish consumption is useful in fetal growth and development due to low saturated and high unsaturated fats, proteins and essential nutrients. However, maternal fish consumption may expose the fetus to environmental contaminants such as polychlorinated biphenyls, dichlorodiphenyl dichloroethylene and methylmercury, which have been linked to neuro-developmental problems in human offspring and structural malformations in animal fetuses. Preliminary findings from the National Birth Defects Prevention Study

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(NBDPS) population suggests that compared to mothers who did not eat fish or ate for less than once a month, mothers who ate 3-5oz of fish, 1-3 times/month were significantly protected for certain birth defects such as oral clefts, anomalous pulmonary venous return and anorectal atresia/stenosis. For other birth defects, as the amount of fish consumed increased to more than 4 times per month, it became a significant risk factor. Therefore women who may conceive, eating 1-3 times fish meals per month might be protective for some birth defects, but it might be less protective to consume high amounts. Our findings are in line with the USFDA recommendations that women of child bearing age eat < 6 of fish ounces a week.

Ammonium perchlorate and pendrin gene expression following exposure during gestation-alone or gestation and lactation. Presenter: Ernest E. Smith, Ph.D., Department of Environmental Toxicology/TIEHH, Texas Tech University

Background: Perchlorate (ClO4-) is a teratogen and disrupts thyroid hormone homeostasis by competitive inhibition of the transport of iodide (I-). Pendrin gene encodes the protein pendrin, which functions as an iodide, chloride and bicarbonate transporter across cell membranes. The objective of this study was 1) to determine the distribution and 2) effects of ammonium perchlorate on pendrin gene expression in the deer mice, a sentinel wildlife species. Method: Deer mice pups were exposed to perchlorate either during gestation-alone or gestation and lactation then euthanized either at postnatal day 21or 45. Taqman specific probe and primers were designed from deer mice cDNA sequence for real-time PCR determination of mRNA content for pendrin. The expression profile was standardized to GAPDH. Results: Pendrin was identified in various tissues of the deer mice. Relative gene expression of pendrin was higher at PND 45 compared to PND 21. Gestational-alone AP exposure resulted in an increased expression of pendrin by more than 2 fold at PND 21 in both treatment groups compared to the control pups. These data suggest that: 1) pendrin is differentially expressed in various deer mouse tissues and appears to be age dependent, and 2) perchlorate alters gene expression in organ systems other the thyroid gland in deer mice following AP exposure during gestation-alone or gestation and lactation. Conclusions: Exposure to perchlorate during the developmental period appears to have postnatal effects at the molecular level.

Maternal Fever during Early Pregnancy and the Risk of Oral Clefts. Presenter: Syed Hasmi, Ph.D., University of Texas-Houston Health Science Center, School of Public Health

Animal studies suggest that maternal hyperthermia is teratogenic and a few studies have implicated maternal hyperthermia as a cause of human oro-facial clefting. However, small sample size(s) and/or inadequate hyperthermic exposure in these studies limited the conclusions and risk assessment. To evaluate the role of maternal hyperthermia in orofacial clefting, we analyzed maternal questionnaire data from the NBDPS. Methods: All orofacial clefting cases born between 1997-2004 were phenotypically categorized. Pregnancies reporting febrile illness were stratified by fever grade and antipyretic use. Logistic regression models were used to generate crude and adjusted odds ratios (ORs) for exposure to fever and association with each cleft phenotype. Results: An increased risk was observed for isolated cleft lip with or without cleft palate after febrile exposure (OR: 1.28, 95% CI: 1.01–1.63). Stratification resulted in significantly higher ORs among women who did not take antipyretics with higher point estimates for non-isolated compared to isolated orofacial clefting cases. Conclusion: An increased risk of clefts was observed among women exposed to fever who did not take antipyretics. This suggests that adequate control of fever diminishes the deleterious effects of hyperthermia.

Oral clefts and proximity to environmental hazards. Presenter: Lucina Suarez, Ph.D., Texas Department of State Health Services

Concerns have been raised about the potential effects that environmental hazards might have on reproductive outcomes. We examined the association between oral clefts and maternal residential proximity to waste sites or industrial facilities. Maternal residences at birth for 1781 deliveries with oral clefts and 4368 comparison births were related to locations of waste sites and industrial facilities in Texas through geographic information systems. Compared with women who lived farther, women who lived within a mile of these waste sites or industrial facilities were not more likely to have offspring with oral clefts. However, among women 35 years or older, oral clefts in offspring were associated with living within a mile of industrial facilities (odds ratio =2.4, 95% CI =2.8-151.0). These findings suggest that maternal residential proximity to industries might

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Research Center

Texas Center Loses CDC Funding

To help reduce birth defects among U.S. babies, in 1996, Congress directed the Centers for Disease Control and Prevention (CDC) to establish the Centers for Birth Defects Research and Prevention (CBDRP). This directive was formalized with the passage of the Birth Defects Prevention Act of 1998 (Public Law 105-168). This act authorized CDC to 1) collect, analyze, and make available data on birth defects; 2) operate regional centers that conduct applied epidemiologic research for the prevention of birth defects; and 3) provide the public with information on preventing birth defects. Since it's inception Arkansas, California, Iowa, Massachusetts, New York, New Jersey, North Carolina, Texas, and Utah, states with existing birth defect programs that had nationally recognized expertise in birth defects surveillance and research, have had participating Centers.

Since 1997, the Texas Center has contributed information about birth defects cases as well as from healthy "control" families in border counties to the National Birth Defects Prevention Study (NBDPS). Since 2004, the study area for Texas was the area known as the Lower Rio Grande Valley, which encompasses Gulf Coast industrial cities such as Corpus Christi, as well as Cameron County, which has experienced some of the country's highest neural tube defect rates and is at the continental U.S.'s south-most point.

In 2001, the Centers participated in a competitive grant application to renew funding; in that round Texas was successful in retaining CDC funding for seven more years. However, in November 2008 we were notified that our competitive application to renew CDC funding for the Texas Center for Birth Defects Research and Prevention, although "approved," was not selected to receive funding. Three of eight existing centers did not receive funding, primarily because of limited funds available for the study.

Texas collaborators have in process about 35 letters of intent or proposals developed to analyze and publish findings on NBDPS data, and will remain active in completing those. We will continue to maintain our Center and much of its infrastructure with academic institutions, but our Center will no longer be part of the National Birth Defects Prevention Study, beginning with deliveries in 2008.

We have celebrated numerous accomplishments over the last 12 years of this grant, bringing approximately $10 million in Federal funding and over 140 peer-reviewed publications to Texas from collaborative population-based birth defects research.

For more information about the Texas Center, contact Mark Canfield, Principal Co-Investigator, at 512-458-7232 Ext. 6158 or mark.canfield@dshs.state.tx.us.

Recent Publications

Bitsko RH, Reefhuis J, Louik C, Werler M, Feldkamp ML, Waller DK, Frias J, Honein M. Periconceptional use of weight loss products including ephedra and the association with birth defects. Birth Defects Res A Clin Mol Teratol, 2008 Jun 13. [Epub ahead of print]

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From the Registry

Focus on Holoprosencephaly

Holoprosencephaly is a brain malformation that is caused by a primary defect in development of the basal forebrain during embryogenesis, causing the brain to develop improperly and resulting in incomplete division of the cerebral hemispheres. The level of non-separation of the cerebral hemispheres indicates the severity of this defect. From most severe to least, the types of holoprosencephaly include alobar, semilobar, and lobar. In alobar holoprosencephaly, there is a single, small ventricular cerebrum without division into hemispheres, a single ventricle, and absent olfactory bulbs and optic tracts. In semilobar holoprosencephaly, there are rudimentary cerebral lobes with partially separated hemispheres. In lobar holoprosencephaly, the central lobes are well developed and the fissure between the hemispheres is distinct, but there is still some fusion of brain structures. Facial anomalies are frequently present, ranging in severity from a flattened nose and closely spaced eyes through a cleft or split lip and a single nostril to cyclopia, where a nose-like proboscis is present over a single eye in the middle of the face. Hydrocephaly or microcephaly is sometimes present. Recently, a fourth type of holoprosencephaly has been described, a mid-hemispheric variant of holoprosencephaly occurs when the rear portion of the brain (posterior frontal and parietal areas) do not separate but the frontal portion of the brain is preserved.

Survival varies depending upon the severity of the defect. However, it is common for surviving children with this defect to manifest a variety of neurological disorders, including cognitive and developmental delays, seizures, motor impairment, and endocrine dysfunction.

According to Leoncini et al. (See Recent Publications, page 7), the worldwide prevalence of holoprosencephaly is 1.3 per 10,000 live births. In Texas, the rate is similar, 1.2. There does not appear to be any geographic variation within Texas (Figure 1). It is more common among Hispanic births (Figure 2) and affects more females than males (Figure 3).

Holoprosencephaly has also been associated with the following (references available on request):

- Foreign-born women (outside of the U.S. and Mexico)
- Early menarche
- Advanced maternal age
- Low socioeconomic status
- Alcohol consumption during pregnancy
- Maternal diabetes

Figure 1 Holoprosencephaly by Region, Texas, 1999-2005

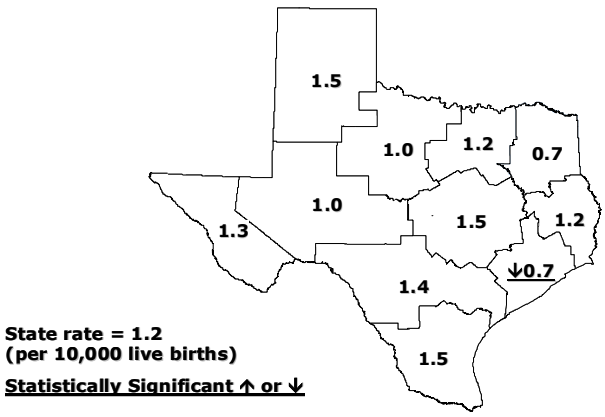


Figure 2: Holoprosencephaly, Texas, 1999-2005

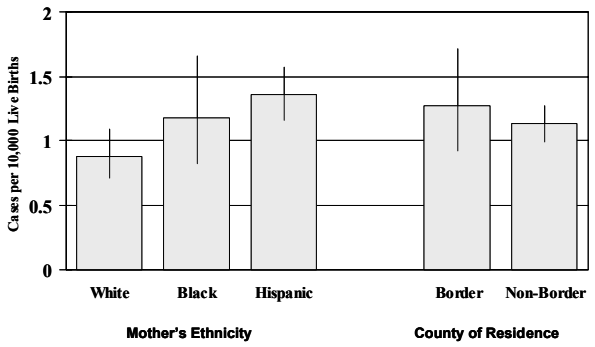
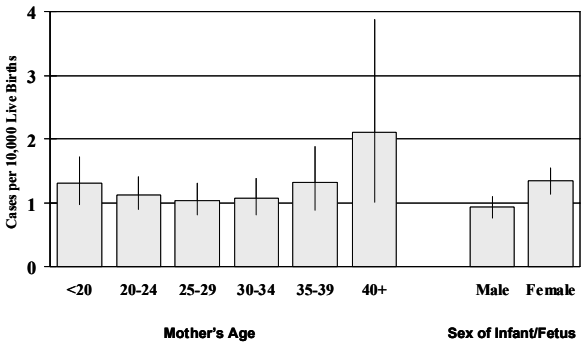


Figure 3: Holoprosencephaly, Texas, 1999-2005



Holoprosencephaly is one of several defects that the Texas Birth Defects Epidemiology and Surveillance staff have identified as a priority for further epidemiologic study. Students or other researchers interested in pursuing this topic should contact Peter Langlois, Ph.D. at 512-458-7232 or peter.langlois@dshs.state.tx.us.

2005 Data Available

Data tables in various electronic formats are now available on the Texas Birth Defects Epidemiology and Surveillance website, www.dshs.state.tx.us/birthdefects/Data/reports.shtm. These data cover birth defects that occurred among deliveries in Texas from 1999-2005 and represent almost 100,000 individual infants/fetuses. It also represents the daily effort and dedication of the fifty field staff who visit hospitals throughout the state to identify affected pregnancies and ascertain important information about the mother and baby.

With the publication of these data, researchers may now request cases from the 2005 deliveries. Individuals interested in using birth defects data should review the data request policies and request form at www.dshs.state.tx.us/birthdefects/Data/access_policy.doc as well as Tips on Using Data from the Texas Birth Defects Registry at www.dshs.state.tx.us/birthdefects/tips_bd_data.shtm

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Prevention

USDA Offers "My Medicines"

It has been estimated that more than 80% of pregnant women take over-the-counter or prescription drugs. Many of these drugs are safe to mother and fetus, and even those with some risk are necessitated by the mother's other medical conditions. Nevertheless, medications can be teratogenic or otherwise harmful during pregnancy, so it is important for women to be aware of which medicines they take and to accurately communicate this information to their health care provider.

The U.S. Food and Drug Administration offers a tool for tracking medications and advice for their proper usage. This tool, a brochure called "My Medicines" can be found in many formats and languages at www.fda.gov/womens/taketimetocare/mymeds.html.

The Cost of Spina Bifida

When planning for prevention programs or policy changes to prevent birth defects, it is often helpful to know whether associated fiscal costs outweigh the direct and indirect costs due to the condition. The Texas Birth Defects Epidemiology & Surveillance Branch has recently prepared a summary of national and state cost data associated with spina bifida. For example, each year, the state of Texas sends $8 million to provide medical treatment for children with spina bifida; more than $6 million is paid by private insurance. To obtain a copy of this document, contact Amy Case at amy.case@dshs.state.tx.us or 512-458-7232.

Lake Madisonville Fish Advisory

The Texas Department of State Health Services has issued an advisory warning people to limit their consumption of largemouth bass from Lake Madisonville. The advisory was issued after laboratory testing showed elevated levels of mercury in the species. No other species of fish from the lake are included in the warning.

Adults should limit consumption of largemouth bass to no more than two 8-ounce servings per month. Children under 12 years old should limit consumption to no more than two 4-ounce servings per month. Women who are nursing, pregnant or *who may become pregnant* should not consume largemouth bass from Lake Madisonville. The brain and nervous system in a developing fetus can be permanently damaged if the mother-to-be eats foods containing elevated levels of mercury during pregnancy.

For more information, contact Michael Tennant, Texas Department of State Health Services, Seafood and Aquatic Life Group, 512-834-6757 or michael.tennant@dshs.state.tx.us.

Living with Birth Defects

Research Opportunity

The Spina Bifida Research Resource (SBRR), at the Texas A&M University System Health Science Center, will soon be inviting families of children born with spina bifida to participate in a research study. The purpose of this study is to find the causes of spina bifida. Participation is free, easy, and involves no travel. Both English

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be associated with oral clefts in births to older mothers.

Proximity of Pediatric Genetic Services to Children with Birth Defects in Texas. Presenter: Amy Case, MAHS, Texas Birth Defects Epidemiology & Surveillance Branch

Families of children with major structural malformations often benefit greatly from genetic services. However, these services are not readily available in all areas of the state, and geospatial disparities occur. For this study, we compared addresses from the Texas Birth Defects Registry for live-born children delivered in 1999-2004 with major structural defects and chromosomal anomalies to the locations of Texas pediatric genetic clinics to determine the distance from case to nearest facility. Although a large majority of addresses at delivery for case families were within 30 miles of the nearest pediatric genetic clinic, there remain important populated areas from which case families would need to drive more than 100 miles to access services.

Increasing message salience to promote folic acid use to women at risk for neural tube defect recurrence during the interpregnancy period: a qualitative approach. Presenter: Tasneem Husain, M.S., Division of Health Promotion and Behavioral Sciences, University of Texas Health Science Center at Houston, School of Public Health

Objective: To develop sensitive print material promoting the use of peri-conceptional folic acid to women at risk for neural tube defect recurrence living in Texas. A brochure was designed using concepts from the Precaution Adoption Process Model (PAPM) and tested by a heterogeneous group of women at risk for neural tube defect recurrence. Methods: Three focus groups comprising 26 mothers of children with spina bifida pretested the brochure. One focus group was conducted in Spanish-only, the other two focus groups were conducted in English and Spanish combined. During brochure assessment, women were asked a series of questions on topics from the Suitability Assessment of Materials (SAM™). Qualitative analysis of coded transcripts revealed key themes and preferences for health promotion material for this population. Results: Women at risk for recurrence expressed a preference for bold, colorful packaging, with high quality materials; and visually preferred realistic, threatening images. While there was little difference in preference for print material between the Spanish-only and the English and Spanish combined groups, there were notable gaps in knowledge and awareness. Women expressed frustration with the bedside manner of their doctors. Although women were not concerned about privacy, they did question the need for a brochure targeting them.A brochure promoting folic acid use during the interpregnancy period to women at risk for recurrence should apply a gain-frame approach and include messages about skills and action. Coinciding with PAPM Stage 3, women respond to threatening images. The women in the Spanish-only focus group were less informed about folic acid.

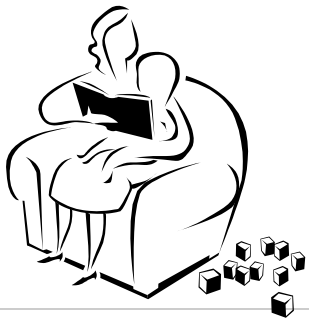
Announcements

Texas March of Dimes Public Policy Priorities

The mission of the March of Dimes is to improve the health of babies by preventing birth defects, premature birth and infant mortality. One of the ways we carry out our mission is through our advocacy efforts. The Texas Legislature goes into session on January 13th and the March of Dimes will be advocating on the following priorities:

1. Support Department of State Health Services Exceptional Item 3, Health Data Collection and Analysis, which includes $1.9 million for the Texas Birth Defects Registry.
2. Support Department of State Health Services Exception Item 11, Chronic Disease Prevention, which includes $2.9 million in general revenue for cystic fibrosis newborn screening.
3. Support Smoke Free Texas legislation.
4. Support 12 months of continuous eligibility for Children's Medicaid.
5. Eliminate the waiting list for children with special health care needs.
6. Support efforts to include smoking cessation counseling services for pregnant women on Medicaid.

For more information on the March of Dimes legislative priorities, please contact Morgan Sanders, State Director of Public Affairs, msanders@marchofdimes.com or visit the March of Dimes website, www.marchofdimes.com/texas.



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and Spanish speaking families can participate. If you would like to refer a family or want more information about the SBRR, please visit their website at www.sbrr.info or contact the Project Coordinator, Barbara Weyland at: 713-677-7573 (local Houston), 866-521-7589 or bweyland@ibt.tamhsc.edu.

Improving Access to Medicaid for Children with Special Needs

The Texas Legislature approved $150 million for the fiscal years 2008-2009 budget period for strategic initiatives to expand children's access to Medicaid services. The new funding is part of a $1.8 billion plan in response to the *Frew v. Hawkins* lawsuit over utilization of preventive services in children's Medicaid. The Frew Advisory Committee reviews proposals and advises the Texas Health and Human Services Commission on which projects should be recommended for funding through the $150 million set aside. Final approval comes from the Governor's Office and the Legislative Budget Board.

The Frew committee has recently recommended funding four more strategic initiatives designed to improve access to health care for children enrolled in Medicaid. One proposal addresses medical home for children with special health-care needs, selecting one HHSC region to serve as a pilot area for a grant program for practices serving children with Medicaid who have special health-care needs that provide a comprehensive medical home for children.

One other proposal – targeted rate increases for pediatric subspecialists – got a favorable reaction from the committee. The Texas Legislature may consider rate increases during the next session.

More information about the Frew committee can be found at www.hhsc.state.tx.us/about_hhsc/AdvisoryCommittees/frew.html.

The Monitor is published twice a year by the Birth Defects Epidemiology and Surveillance Branch, Texas Department of State Health Services:

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DSHS Pub. No. 58-10955

Calendar

2009

February 18: 2009 Center for Health Promotion and Disease Prevention Research in Underserved Populations Conference. Health Disparities: From Local to Global, Austin. Contact: 512-471-9910, CHPR@mail.nur.utexas.edu, www.utexas.edu/nursing/chpr/conference.html

February 23-25: National Birth Defects Prevention Network Annual Meeting, Nashville. Contact: Cara Mai 404-398-4918, cwm7@cdc.gov.

March 10-12: 8th Annual Forum for Improving Children's Healthcare, Grapevine. Contact: 866-787-0832, www.nichq.org/nichq

March 15-18: First World Congress on Spina Bifida Research and Care, Orlando. Contact: Russ Kirby, rkirby@uab.edu. http://medicalconference.spinabifidaassociation.org

April 15-17: Texas Public Health Association 2009 Annual Education Conference. Contact: txpha@aol.com, www.charityadvantage.com/texaspha/Home.asp

May 3-5: Achieving Success in Women's Health, Fort Worth. Contact: 303-771-4044, snowinst@eazy.net www.snowinst.com/womens-health-conference.htm.

May 28-29: 4th Annual Texas Conference on Health Disparities. Ft. Worth. Contact: www.hsc.unt.edu/HealthDisparities/conference.html

June 28-30: TxHIMA Annual Meeting & Convention, Dallas. Contact: 512-392-4715 txhima@txhima.org..org

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